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UPDATE ON JAPAN'S BIOTECHNOLOGY INDUSTRY: STUNTED GROWTH?

Summary

Mirroring developments in the U.S. industry, an increasing number of Japanese biotechnology firms are putting real products on the market. At the same time, more and more companies are entering the biotechnology field, translating into increasing amounts of money devoted to research. The government is trying to keep up with the fast moving industry, both in terms of research outlays and regulatory policy.

Despite all this activity, many observers have been disappointed with the pace of development in Japan. Others feel that Japan is right on schedule toward building a world-class industry. This examination will update Japan's technological and regulatory progress since JEI's last analysis (see JEI Report No. 8A, February 24, 1984).

Overview of Biotechnology

Biology was once mainly a descriptive science -- researchers classified the many types of organisms and noted gross and microscopic traits. In recent decades, however, biologists have begun to understand the causative mechanisms underlying their observations, raising the tantalizing possibility of modifying and manipulating biological phenomena. The discovery that the organization of molecules into cells and then into organisms is dictated by a blueprint contained in long sequences of nucleic acids known as deoxyribose nucleic acid, or DNA, opened the door to a new age of active biology.

Although traditional biological techniques, including selective breeding and hybridization, have been used to modify the DNA code or genes of plants and animals, they are indirect, imprecise and time consuming. Armed with an understanding of what nucleic acid sequence produces a particular biological result, biotechnologists can directly manipulate or introduce new sequences into a cell's genetic code, producing almost immediate results.

The possibilities are endless, ranging from improved plant and animal varieties to new and less costly drugs and biological compounds, energy sources, industrial processes and even organic computers. The problems, however, are equally impressive. Identification of genetic sequences, as well as how genes interact with each other, is still in the early stages of development. Techniques to grow desirable cells outside of the parent body, to insert, activate and deactivate genes, and to process and recover the sought-after biological compounds have advanced to the commercial application stage, but there remains much room for improvement. Finally, researchers and entrepreneurs are beginning to delve more deeply into the ethical and environmental questions posed by the power of biotechnology.

Industry in Ferment

In JEI's first study on this subject, biotechnology fever was just beginning to spread in Japan. Although government agencies and a few companies had established biotechnology programs as early as 1979, interest in it did not spread to a wide range of industries until 1984. At that time, it appeared that the long-range benefits of biotechnical expertise outweighed the risks. Oil, chemical, glass, food processing and pharmaceutical firms caught the biotech bug, and many of Japan's new venture businesses also entered the field.

With the market for biotechnology products estimated at Y50 billion ($250 million at Y200=$1.00) this year, the incentive is strong. The outlolk for the industry is even more enthusiastic. Private analysts see the market growing to as much as Y5-Y8 trillion ($25-$40 billion) in 15 years, while various government agencies see the development of markets as large as Y15 trillion ($75 billion) by the beginning of the next century (see table).

The Ministry of Agriculture, Forestry and Fisheries reported that as of mid-1985, 389 companies and research institutes were engaged in biotechnology projects, of which 179 were private businesses and 210 were government-sponsored. The MAFF survey revealed that most of the private companies were focusing on pharmaceutical or food applications, while government laboratories were engaged in more esoteric applications, such as biosensors and biocomputers. On average, each private firm employed 19 researchers or engineers for each biotech project, far more than government institutions which reported an average staff of two. Many private-sector firms reported that they were actively collecting and analyzing genetic resources: an average of 2,000 samples of seeds and microbes had been gathered at the time of the survey. These efforts were augmented by collection programs at the local government level, which in some cases totaled as many as 1,500 samples.

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The Impact of Biotechnology on Japanese Products by the Year 2000

(in billions of yen)

Product	Production	Value Added
Rice and Grain	Y519	Y381
Vegetables	257	164
Fruits	13	9
Root Crops	13	8
Beverages	2	1
Food Products	91	66
Tobacco	12	9
Seeds	494	400
Dairy Farming	327	111
Meat	146	37
Wood Products	9	7
Fisheries	118	71
Copper Ore	17	13
Iron Ore	15	11
Nonferrous Ores	2	1
Petroleum	0	0
Dairy Products	590	150
Bread and Cakes	1,370	507
Sugar	108	13
Plant Oils	0	0
Flavorings	251	73
Animal Feeds	637	58
Alcoholic Beverages	1,113	662
Wood Pulp	90	17
Ammonia	17	4
Ethyl Alcohol	Y164	Y49
Methanol	52	14
Industrial Oils	75	19
Basic Petrochemicals	317	44
Other Petrochemicals	753	116
Textile Fibers	80	23
Fertilizers	0	0
Farm Chemicals	142	33
High-Pressure Gas	64	28
Other Basic Chemicals	73	34
Pharmaceuticals	3,151	1,564
Cosmetics	466	155
Consumer Chemicals	479	149
Oil Products	463	79
Electrical Copper	58	4
Nonferrous Products	242	46
Computers	188	80
Electronic Goods	287	103
Integrated Circuits	98	42
Medical Equipment	31	15
Propane	0	0
Underground Waterworks	479	303
Aboveground Waterworks	420	238
Waste Management	471	349
Total	15,003	6,312

Source: Ministry of International Trade and Industry

R&D Multiplies

As for research and development outlays, a Nihon Keizai Shimbun survey of 268 private companies shows extremely rapid growth. The companies queried are spending an average Y295 million ($1.5 million) on biotechnology projects in FY 1985 (ending March 31, 1986), a 51.5 percent jump over fiscal 1984, which itself represented a 28.2 percent increase. At the top of the company list is Mitsubishi Chemical Industries Ltd., with a FY 1985 budget of Y10 billion ($50 million). Furthermore, 41 percent of the companies expect to build or expand biotechnology facilities and, equally important, 74 percent intend to hire more researchers. As an indication of the relative youth of the field, only 52 percent of the respondents presently have facilities devoted solely to biotechnology research and these are staffed by just 17 people on average.

An October 1985 Ministry of International Trade and Industry survey presents older, but more comprehensive, data. Japanese industry spent a total of Y334.8 billion ($1.7 billion) in fiscal 1983 on biotechnology research, a 13.7 percent gain from the previous year. Not surprisingly, the manufacturing sector accounted for almost 99 percent of these expenditures. The chemical industry ranked first at Y280.7 billion ($1.4 billion), with pharmaceutical makers alone spending Y221.8 billion ($1.1 billion) on R&D; next came food processors with Y29.8 billion ($149 million). These figures represent growth rates of between 12.2 percent and 16.3 percent.

Although a general idea of the direction of Japanese biotechnology R&D can be gleaned from the preceding industry analysis, the picture is incomplete since many companies are using biotechnology to diversify into other lines of business. For example, Asahi Breweries Ltd. is pursuing the development of circulatory drugs, diagnostic kits and biosensors, as well as improved beer yeasts. Generalizations about the thrust of particular industries can still be made, if one also keeps in mind this trend toward diversification.

- Pharmaceuticals - Cancer diagnosis and treatment are the main targets of drug companies' biotechnology efforts. Alpha and gamma interferon, various interleukins, monoclonal antibodies and a tumor necrosis factor are being developed by several firms, and some have begun the long Health and Welfare Ministry approval process.

- Basic Chemicals - This group exhibits the most diverse projects, ranging from the more efficient production of basic chemical stocks to anti-pollution applications, food products and drugs. The only real generalization that can be made is that these firms seem to be looking for relatively quick returns on their investments to compensate for mature or sagging traditional markets. Licensing technology has been the usual pattern of development in this sector, although original R&D efforts are growing.

- Food Processors - After an initial wave of development directed at improving existing lines of business, food companies are beginning to expand into mass production of biological compounds. Growth hormones, blood-clotting factors, and other blood serum components are thought suitable for mass production via biotechnology. Research on more complex products, including monoclonal antibodies and tissue plasminogen activator (a blood-clot-dissolving compound), is also being pursued.

• Agriculture - Research aimed at improving terrestrial and marine plants as well as animal species is just beginning. Unlike U.S. researchers, Japanese horticulturalists have been somewhat slow to pursue the more daring options available through biotechnology, namely the insertion of foreign genetic material into plant cells. Recent plant introductions have offered yield improvements without significant departures from the basic plant stock. With increasing use of cell fusion techniques and the discovery of suitable vectors to introduce new genes into plant cells, Japan hopes to become a major player in the agri-products market by the next century.

• Electronics - This unlikely group is interested in the more esoteric biotechnologies, including biosensors and biocomputers. These areas of research are so risky that cooperation with the government is the norm. A more detailed discussion follows in the section on government policy.

An overall pattern is discernible in the development of Japan's industry that is not surprising. Most of the initial efforts have gone into areas where the country's strong tradition of excellence in fermentation could be applied -- continuous and large-batch production methods, and food- and drug-related applications. Now, however, the Japanese are beginning to expand into other areas they consider vital to future economic growth, leading to a heavier emphasis on basic research.

The Bottom Line

Now that they are several years old, a comparison of the financial data of U.S. and Japanese biotechnology firms is possible but must take into account the fact that many Japanese entrants often derive much of their income from non-biotechnology businesses. Direct company-to-company comparisons are therefore difficult, although not for major pharmaceutical firms (see JEI Report No. 45A, November 22, 1985). Nevertheless, it can be seen that biotechnology is becoming profitable. Several Japanese firms that produce assay or diagnostic kits as well as those that produce therapeutic biological compounds have hinted strongly that development costs are now being recouped. On this side of the Pacific, several biotechnology startups have announced their first profitable year, including Genentech Inc., Cetus Corp. and Applied Biosystems Inc. The increasing number of takeovers or mergers between biotechnology firms and other companies is also evidence of a better financial outlook.

For analytical purposes, stock prices can serve as a rough substitute for financial results. Several private indices of biotechnology stocks exist for both the Tokyo and New York Stock Exchanges. Unfortunately, these measures are also full of caveats. First, the companies included in each index may not be comparable, like apples and oranges. This shows up most clearly between the Japanese and American biotech indices because the Japanese tally the results of diversified companies such as Asahi Chemical Industry Co., Ltd., Mitsubishi Chemical Industries and Dainippon Pharmaceutical Co., Ltd., while in the United States, only pure biotechnology companies, such as Genentech, Centocor Inc. and Hybritech Inc., are included. There is also the question of which index to use. On the American side there are at least three: Paine Webber's, Kidder, Peabody & Co.'s and one put out by Bioengineering News, San Francisco, California. Across the Pacific, the picture grows more complicated.

Practically every major securities house has its own biotechnology index, in addition to an informal one followed by Nihon Keizai Shimbun.

Although details may differ, all show great variability in the stock price of biotechnology firms. According to Bioengineering News' Bioaverage, for example, the average stock price of three dozen U.S. biotech firms fell pretty steadily between April 1981 (a beginning value of 100) and August 1982 (when it rested at 59.60), rose through June 1983 (to 149.56), dropped again until December 1984 (to 71.37), then worked its way back up by December 1985 (107.67).

On the Tokyo Stock Exchange, where wide swings are much more the norm, the Nikkei biotech average has been extremely unstable. Although other factors are always involved, the average has diverged from the surges and ebbs of the overall market, often by wide margins. As the overall Tokyo exchange average leapt nearly 500 points between May 1984 and August of the same year, the biotech average moved up almost 700 points, then plunged almost 1,000. In 1985 both averages were better behaved, the overall index rising relatively steadily, while the biotech index made forward, but still erratic, progress.

International Genes

Joint ventures and international markets are an increasingly prominent feature of the Japanese and American biotechnology industries. Much of the activity is due to the extremely high cost of developing and marketing new products, especially pharmaceuticals. Many small U.S. biotechnology venture companies are tying up with large established firms, combining technology with production, distribution and marketing know-how. Foreign firms have been eyeing the Japanese market, which is second only to that of the United States, and recent government trade liberalization programs, particularly the acceptability of foreign clinical test data, have improved the chances of gaining a foothold. In addition to cost and market scale considerations, companies realize that technology knows no national boundaries. Japanese firms have long made excellent use of foreign technology, and foreigners are taking increasing advantage of what Japan has to offer. Companies involved in these joint ventures and technology exchanges are listed in an appendix to this report. The list is not meant to be exhaustive, but rather indicative of industry trends.

It is clear that U.S. biotechnology firms have been aware of the benefits of international cooperation for some time. At the beginning of the 1980s, U.S. firms were clearly ahead of their Japanese rivals but ready to share development costs with larger partners. This pattern of foreign money funding the development of U.S. technology has become widespread in recent years, although it does not necessarily translate into manufacturing or marketing rights. The appendix shows how both American and Japanese companies respond to the actions of domestic rivals. U.S. companies seem to be in a race to find large partners to pump cash into their operations, while Japanese firms are racing to obtain rights to cutting-edge technology. Finally, the appendix also shows a rise in the number of commercialization agreements heralding the appearance of biotechnology products in the marketplace.

Unlike other industries, therefore, biotechnology is developing as a global community, and a rapidly growing one at that. Japan's biotechnology

market is certainly not lacking private-sector impetus, but the government is also contributing its fair share.

Shepherding Japan's Biotechnology Flock

Despite a program of stringent fiscal austerity, Tokyo continues to strengthen its support for biotechnology and other crucial research areas. While overall discretionary spending has decreased slightly in the past two fiscal years, funds for biotechnology programs within various government agencies have expanded at rates from 15 percent to 18 percent annually. For fiscal 1985, Tokyo will spend an estimated Y49.4 billion ($247 million) on biotechnology research, regulation and administration. Direct research expenditures remain relatively small, with much of the money that has been earmarked for life sciences funding operations of university departments, government institutes, administrative costs and gene banks. At the present time, one major thrust of government support is the creation of gene banks and the pooling of research data via an electronic network.

Leading the list in terms of spending is the Ministry of Education with outlays of approximately Y20 billion ($100 million), the vast majority of which flows into national research institutes and universities. MOE was first to take an interest in biotechnology and has been collecting genetic material and supporting research and education activities through the National Institute of Genetics since the late 1950s. At present, MOE is underwriting more than 80 gene bank projects: 23 related to animals, 27 on plants, 30 concerning microorganisms, and approximately 10 involving animal cells. Researchers at various universities are engaged in a wide range of studies on biosensors, synthetic cells and recombinant DNA technology.

In second place is the Ministry of Health and Welfare with a budget of approximately Y12 billion ($60 million). The bulk of these funds supports the complex pharmaceutical testing and approval system that is the bane of both domestic and foreign drug firms. MHW operates the National Institute of Health (patterned after the U.S. National Institutes of Health), the National Institute of Hygenic Sciences (patterned after the U.S. Centers for Disease Control) and several research centers located at Tsukuba Science City, north of Tokyo. The burden of developing safety guidelines for biotechnology research also falls on MHW's shoulders, although the Ministry of International Trade and Industry also has a say. In addition to a handful of small projects within NIH and NIHS, the ministry is beginning to fund some modest industry cooperative projects concerned with cancer treatment, including alpha interferon and interleukin-2. Finally, the agency also established a gene bank in 1984 to collect genetic material and establish collection guidelines, catalogue and offer a database on genes in the collection.

Next in line is the Ministry of Agriculture, Forestry and Fisheries with a budget of about Y10 billion ($50 million) for fiscal 1985. In cooperation with Kikkoman Corp., MAFF is trying to develop a cell fusion process to produce fertile hybrid plants. Similarly, a project with Kirin Brewery Co., Ltd. is aimed at faster development of hybrid seeds. A group of 14 private companies is exploring other cell fusion techniques with MAFF footing most of the projected Y30 billion ($150 million) cost of the eight-year program. To provide more direct aid, MAFF is planning to establish a biotechnology promotion center

in fiscal 1986 with funds from dividends paid to the government by the recently privatized Japan Tobacco Inc. Its first-year goals include low-interest loans to 20 projects, accounting for most of the initial budget of Y5-Y6 billion ($25-$30 million). However, the project's outlook remains clouded due to fiscal considerations.

MAFF's National Institute of Agrobiological Resources has been carrying out biotechnology research since 1983. With a staff of 123 researchers, the institute's fiscal 1985 budget is a little over Y2.5 billion ($12.5 million). One of its projects has already yielded fruit; a patent is being sought on a new, heavier-bearing hybrid rice. Other research topics include plant virus studies and the mechanics of plant cell mutation and photosynthesis. MAFF's gene bank program is probably the most extensive, with repositories at NIAR, the Forest Experiment Station, the Vegetable and Ornamental Crop Research Station, the Fruit Tree Research Station, the Sericulture Experiment Station, the National Research Institute of Tea and 17 National Livestock Breeding Stations.

The Ministry of International Trade and Industry's biotechnology budget is only about Y4.2 billion ($21 million) this fiscal year, but because it is not burdened with administrative duties, it actually funds an equivalent amount of research as the previous ministries. More importantly, much of the MITI-sponsored research is conducted in cooperation with private firms and concentrates on commercial applications of biotechnology.

Under the Research and Development Project on Basic Technology for Future Industries, a 10-year program begun in 1981, bioreactors (immobilized enzymes, subsitution of enzymes for catalysts and recycling of co-enzymes), large-scale cell cultivation (suspension culture, culture of epithelial cells and differentiation cultures) and recombinant DNA applications (high-oxidation and secretory microorganisms) are being developed. The Fermentation Research Institute also funds various research projects, but is equally interested in establishing a Patented Microorganism Depository. As Japan's only designated international patented microorganism institute (under the Budapest Agreement), the facility can house at least 7,000 strains of microorganisms and hopes to become an important part of the international biotechnology industry.

Organic electronics, including biocomputers, seem to have caught the fancy of MITI planners. The Japan Key Technology Center, a non-profit organization established by MITI, has recently joined forces with five Japanese companies to develop techniques to modify natural proteins for use in bioelectronics. In addition to providing one-third of the research staff, the government may lay out up to 70 percent of the 10-year project's Y30 billion ($150 million) budget. Mitsubishi Chemical Industries, Takeda Chemical Industries Ltd., Kyowa Hakko Kogyo Co., Ltd., Toray Industries Inc. and Toa Nenryo Kogyo K.K. will provide the remaining funds and personnel. MITI also wants to spend Y8 billion ($40 million) over the next decade on an organic computer modeled after the human brain. As part of this program, NEC Corp. and MITI's Electrotechnical Laboratory have begun work on bioelectronic circuits, the first step toward an analog computer.

MITI is also involved in promoting biotechnology businesses through the Office of Biotechnology and the Venture Enterprise Center. The former acts as

a clearinghouse for technical information while the latter helps startup firms with capital and management consulting.

The Science and Technology Agency, part of the Prime Minister's Office, is also heavily involved in biotechnology research. With a biotechnology budget slightly less than MITI's, STA suppports several domestic and international programs, of which the most prominent is the Institute of Physical and Chemical Research (RIKEN). With facilities in several locations, including Tsukuba, RIKEN is at the forefront of biosensor developments. It also opened a maximum security containment facility (P4 level) for recombinant DNA work in September 1985.

Government biotechnology research and development activities are focused on commercialization in several key areas. This approach, however, has been criticized as Japan nears the frontiers of technology. There is a growing awareness that support for broad basic research must be improved if Japan is to catch up with the United States and Europe in non-fermentation fields.

Keeping the Flock Under Control

Regulatory policy is becoming increasingly crucial as more and more products near the commercialization stage. The details of the issues involved are complex and esoteric, but the overall problems can be easily grasped. Japan is actually having a somewhat easier time of developing regulations than the United States because it tends to rely heavily on American models. Moreover, because Japanese industry is not engaged in the more unusual applications of biotechnology, the regulatory problems are lighter.

In general, MITI and MHW have been cautious about approving human-related applications, but accommodative to industrial uses. MITI is committed to making Japan a top-flight competitor in biotechnology, while MHW continues to refuse risking the nation's health. The extent of Japan's regulatory web is probably second only to the United States. After a year of study by a semi-public advisory council, the Ministry of Education adopted recombinant DNA experiment guidelines in early 1979. The Science and Technology Agency followed with nearly identical regulations later that year. These initial rules were considered more stringent than those followed by the U.S. National Institutes of Health, although this did not present a problem since research was just getting under way.

Within a few years, however, revisions had become necessary to keep abreast of maturing technologies. By mid-1983 significant changes had been made in the original guidelines in regard to large-scale experiments and allowable hosts and vectors for recombinant DNA work. If the organisms involved present relatively low risks (physical containment levels P1 and P2), experiments can proceed without government approval. More dangerous microbes (levels P3 and P4) require government supervision as well as permission.

A number of leading-edge experiments are currently prohibited, although approval may be granted on a case-by-case basis. Chief among these is a ban on the deliberate release of modified microorganisms into the environment. A similar rule is in effect in the United States and lies at the center of heated debate and litigation. There are probably upward of 100 experiments awaiting

approval from the Environmental Protection Agency, some privately sponsored, others as components of government programs. (The U.S. Department of Agriculture alone has 80 to 90 release experiments lined up.) At present, no Japanese companies are contemplating this kind of experiment, but Japanese officials are concerned that domestic companies will soon seek such permission and are wrestling with additional guidelines.

As for plant and animal experiments, guidelines published by MOE in February 1984 are extensive, though apparently not to the point of hindering research. In addition to those projects mentioned earlier, experiments involving human cancer-causing genes in mice and bacterial and pathogenic genes in plants are in progress.

The greatest regulatory barrier to biotechnology products is the maze of pharmaceutical regulations maintained by the Health and Welfare Ministry. Foreign drug companies have shown increasing interest in Japan's market and the recently concluded sectoral negotiations between the United States and Japan yielded some significant changes. MHW's willingness to accept foreign clinical data if racial differences are not a factor is probably the most important policy shift (see JEI Report No. 2B, January 17, 1986). This, along with other procedural changes, should hasten the approval process and improve relations between the ministry and foreign drug manufacturers.

Although MITI is on the verge of releasing industrial biotechnology guidelines, it may wait for the Organization for Economic Cooperation and Development's Committee for Scientific and Technological Policy to adopt a single set of biotechnology guidelines this month. The Japanese delegation was successful in arguing that the regulations should not hinder large-scale industrial and agricultural uses of biotechnology, since only well-tested processes and relatively harmless products are involved. Not only will uniform international regulations make MITI's job easier, it will probably speed the global introduction of biotechnology products.

The development of safe and flexible guidelines is still at an early stage. Means of judging the long-term impact of experiments both on subjects and the environment are in the formative stage, to say nothing of the delicate ethical questions involved, including somatic therapy and gene screening.

Thoughtful Problems

Equally important and difficult are questions concerning intellectual property policy. In view of the many millions of dollars expended to develop and bring a biotechnology product to market, businessmen are naturally interested in protecting their investment. Since useful genes can be produced with relative ease if one knows the proper sequence, the temptation to copy publicly announced developments is strong. In fact, companies no longer display exact genetic sequences at press briefings out of concern for such illegal reproduction. So far, policymakers have turned to existing copyright and patent laws to develop legal protections -- copyright law to cover specific products and patent law to safeguard the underlying technology.

An oil-eating microbe engineered by Dr. Ananda Chakrabarty of General Electric Co. became the first patented microorganism on June 16, 1980 after

eight years of litigation. The decision was a major extension of patent law to cover living organisms and helped foster the growth of the American industry. On October 10, 1985, the patent mantle was expanded again to include genetically engineered seeds, plants and plant tissues. Plants produced by traditional sexual and asexual techniques have been granted patent protection in the past, but a U.S. Patent Office decision could have a major impact on the $3 billion seed business. Genetic engineers can now patent and license a new plant while it is still in the test-tube stage, possibly generating enough revenue to fund its commercialization.

While microorganisms have been patentable in Japan since 1979, Tokyo is in the midst of amending the patent law to include genetically engineered microorganisms. Unfortunately, agreement between the various ministries and the private sector is proving to be elusive. Prior to August 1985, new plant varieties (however produced) were eligible for protection under the Seed and Sapling Law of 1978, and in some cases the patent law. The Patent Office and the Ministry of Agriculture agreed, however, that all new plant breeds would be excluded from patent protection. Under the Seed and Sapling Law, only the method used to develop the new breed can be protected. A Japanese farmer who plants registered hybrid seeds, for example, would be free to use any seeds harvested to replant next year's crop. Commercial sale of registered seeds, however, remains the exclusive right of the developer.

In an effort to promote a global industry, the OECD issued a report in October 1985 recommending improved protection for biotechnology products. The principal points are:

- Inventors should be granted a grace period during which patent claims can be submitted at the international level.
- Microorganisms per se should be patentable.
- Naturally occurring microorganisms should be patentable if newness and industrial applicability can be proved.
- Deposit or description of microorganisms should complement repeatability (of an experiment) requirements.
- Guidelines must be developed covering the release of microbes.
- Protection for plant materials should be improved.
- Inanimate products of nature should be patentable.
- Patent office procedures should be expedited.
- Academic researchers should be encouraged to patent results.
- More systematic study must be given to infringement penalties.

Whether these OECD guidelines will help produce uniform international protection is unclear.

Outlook

To summarize, Japan's biotechnology industry has made steady progress. By parlaying their strength in food fermentation into positions as manufacturers of biotechnology products, Japanese companies are positioning themselves for a long-range development program that could put them at the top of the heap. The government is trying to foster this trend with judicious applications of money and the careful construction of regulatory and intellectual property policies. Nevertheless, the industry continues to exhibit major weaknesses.

By focusing on applications with immediate commercial use, Japanese companies may be neglecting the bolder experiments that could be the key to future leadership. Although the incremental approach has served them well in the past, the chances of being left even farther behind are not insignificant. An increased national emphasis on basic research should help ameliorate this situation, but time considerations may make gradual improvements moot.

Decidedly absent from Japanese efforts is work on outer space biotechnology. Several processing experiments aboard the U.S. space shuttle have proven the value of a micro-gravity environment, but Japanese firms have not reserved space on any scheduled space flight. Given the U.S. lead in space flight, it is understandable that the contrast appears lopsided. Beside producing a module for the U.S. space station, the government is just beginning to organize private groups to commercialize space. If Japan fails to gain significant space processing experience before the turn of the century, any original advantages may be nullified.

In recognition of these weaknesses, international cooperative programs are being launched by the government and private industry. Japan and France inked an agreement in April 1985 to exchange genetic resources as the first step toward full cooperative research. In December of that year, the Institute of Physical and Chemical Research also established a global data center and repository for microbes as part of the World Federation for Culture Collections. The center's goal is to store 500,000 to 600,000 strains of microorganisms and provide global access via telephone beginning in 1987. Finally, MITI is encouraging the Bio Industry Development Center to widen its membership and establish exchange programs with counterparts in the United States and Europe. Through BIDEC, MITI will also try to fund research in foreign as well as domestic universities. The realization that only through true internationalization can Japan's biotechnology industry prosper into the next century is rapidly becoming a policy keystone. Although a host of obstacles remain to be overcome, Japan's biotechnology industry has yet to show signs of stunted growth.

For further information, contact Jon Choy.

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The views expressed in this report are those of the author and do not necessarily represent those of the Japan Economic Institute.

Appendix

Examples of International Joint Ventures and Technology Exchanges in the Biotechnology Field

- Collaborative Research Inc. and Green Cross Corp. of Japan decide to cooperate on interferon development. (February 1981)
- Genex Corp. and Mitsui Toatsu Chemicals Inc. agree to work to produce urokinase (a clot-dissolving enzyme) via biotechnology. (June 1981)
- Enzo Biochem Inc. sells worldwide marketing rights to its monoclonal antibody-based diagnosis kits to Meiji Seika Kaisha Ltd. (May 1982)
- Shionogi & Co., Ltd. and Biogen Inc. begin gamma interferon cooperative research. (June 1982)
- Genentech Inc. and Mitsubishi Chemical Industries Ltd. begin cooperative research on producing human serum albumin through recombinant DNA techniques. Mitsubishi subsequently obtains license to sell Genentech's tissue plasminogen activator technology in the Japanese market. (May-June 1982)
- Teijin Chemicals Ltd. funds monoclonal antibody research by Hybritech Inc. in exchange for marketing rights in Japan and the Far East. (November 1982)
- Biogen Inc. begins an agreement spree with Japanese companies. Recombinant DNA technology for producing Factor-VIII went to Teijin Ltd.; tissue plasminogen activator know-how to Fujisawa Pharmaceutical Co., Ltd.; hepatitus-B vaccine research to be conducted with Green Cross Corp.; and interleukin-2 to be developed with Shionogi & Co., Ltd. (Starting January 1983)
- Integrated Genetics Inc. sells marketing rights to recombinant DNA diagnostic compounds to Fuji Rebio Inc. and tissue plasminogen activator to Toyobo Co., Ltd. (March 1983 and November 1983)
- Genex Corp. and Yoshitomi Pharmaceutical Industries Ltd. begin cooperative research on producing interleukin-2 via engineered microbes. (July 1983)
- Toyo Soda Manufacturing Co., Ltd. supports research on monoclonal antibodies for cancer diagnosis by Hybritech Inc. (November 1983)
- Genentech Inc. licenses Fujisawa Pharmaceutical Co., Ltd. to market the U.S. firm's tumor necrosis factor in Japan. (June 1984)
- Sumitomo Chemical Co., Ltd. buys rights to develop Biogen Inc.'s Somatomedin-C in Japan. (June 1984)

- Sankyo Co., Ltd. agrees to fund development of tumor necrosis factor and macrophage activating factor by Great Britain's Celltech Inc. (October 1984)

- Chugai Pharmaceutical Co., Ltd. funds development of erythropoetin by Genetics Institute Inc. (November 1984)

- Plant Genetics Inc. begins work on synthetic seeds with Kirin Brewery Co., Ltd. (January 1985)

- LKB-Produkter AB of Sweden establishes a Japanese subsidiary to sell its medical analysis equipment using biotechnology. (January 1985)

- Suntory Ltd. purchases manufacturing and marketing rights to Schering-Plough Corp.'s gamma interferon technology. (February 1985)

- Takeda Chemical Industries Ltd. buys alpha interferon technology from Genentech Inc. (February 1985)

- Integrated Genetics Inc. sells marketing rights to its erythropoetin to Toyobo Co., Ltd. for all areas other than the United States and Europe. (February 1985)

- Toray Fujibionics Co., Ltd. will fund research at Centocor Inc. in exchange for marketing rights to Centocor's oncogene (cancer-related) products. (March 1985)

- G.J. Ball Inc., a Chicago-based seed company, joins Toyo Menka Kaisha Ltd. and Mikado Seed Growers Co., Ltd. in developing and growing hybrid seeds. (March 1985)

- Toyo Menka Kaisha Ltd. will help Britain's Cogent Ltd. introduce its biotechnology into Japan, including tissue plasminogen activator, pro-urokinase and an anti-thrombolitic agent. (June 1985)

- Otsuka Pharmaceutical Co., Ltd. opens a research facility in Rockville, Maryland, the first such Japanese presence in the United States. (June 1985)

- Yamasu Shoyu Co., Ltd. sells its monoclonal antibody know-how to Celltech Ltd. (July 1985)

- Biogen Inc. agrees to let Suntory Ltd. market its tumor necrosis factor in Japan. (November 1985)

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